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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,478	02/04/2005	Dramane I. Laine	P51368	3653

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/523,478	LAINE ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute; cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 7* is/are pending in the application.

4a) Of the above claim(s) *4-6,8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement (IDS) submitted on filed February 13, 2005 have been received and acknowledged.

Response to restriction

Applicant's election with traverse of group I claims 1-3 and 7 in the reply filed on February 13, 2006 is acknowledged. Claims 4-7 and 8-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. The traversal is on the ground(s) that the technical feature is provided by common utility and the special technical feature is provided by formula I. This is not found persuasive because as stated in the office action mailed 12/09/05 the compound is already known in the art. The standard for breaking lack of unity among other things is that the compound is known compound.

The requirement is still deemed proper and is therefore made FINAL. Claims may be rejoined if no art is found and if the claims to be rejoined are of identical scope and free of prior art.

Status of Claims

Claims 1-3 and 7 were elected and claims 4-6 and 8-9 are withdrawn from further consideration.

Claims 1-3 and 7 are pending.

Claims 4-6 and 8-9 are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the compound according to formula I is used for the treatment of....?

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear which group R3 is selected from is it the group before the semicolon or the group after?

> **R3 is selected from the group consisting of hydrogen, C_{1-5}alkyl, cycloalkyl, cycloalkyl C_{1-5} alkyl, C_{2-4}alkenyl, C_{2-4}alkenylaryl; cycloalkyl C_{1-5} alkyl, and C_{1-4}alkylaryl, which may be optionally substituted independently by a substituent selected from the group consisting of halogen, nitro, halosubstituted C_{1-4} alkyl, C_{1-4} alkyl, amino, mono**

How can $R(2)_0$ be interpreted, is it a zero, an O?

The claim set forth by election compound [2—(4-chloro-thiazol-2-yl)-phenyl]-carbamic acid piperidin-4-yl-methyl ester. However failed to show how it was made in the specification.

Claim 1 also recites n is 1 or 2; and independently. What does and independently mean?

Claim 2 is unclear as to which group R3 is selected from is it the group before the semicolon or the group after?

Should the compound in claim 2 read [2—(4-chloro-thiazol-2-yl)-phenyl]-carbamic acid piperidin-4-yl-methyl ester or [2—(4-chloro-thiazol-2-yl)-phenyl]-carbamic acid piperidin-4-ylmethyl ester?

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 7 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making compounds of thienyl carboxylate esters, does not reasonably provide enablement for using all thienyl carboxylate esters. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The factors considered in making the enablement rejection have been 1) Nature of invention.

2) State of prior art.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

4) Level of predictability in the art.

5) Amount of direction and guidance provided by the inventor.

6) Existence of working examples.

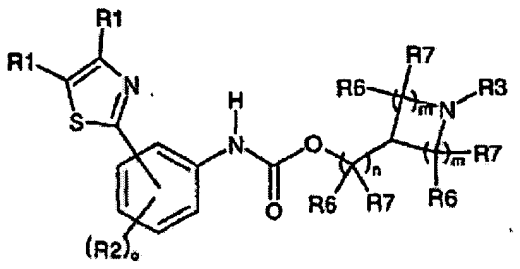
7) Breadth of claims.

8) Level of ordinary skill in the art.

See below:

1) Nature of the invention.

The nature of the invention is directed to compounds of M3 muscarinic acetylcholine receptor antagonist having a core structure



(I)

. As stated, however, claim 1 includes within its scope, all compounds with general core structure in a pharmaceutical composition to treat with expectation of success chronic obstructive lung disease, chronic bronchitis, asthma pulmonary fibrosis, gastroduodenal ulcers urinary track disorders etc.

2) State of the prior art and the predictability or lack thereof in the art.

The state of the prior art is that it involves a myriad of diseases such chronic obstructive lung disease, chronic bronchitis, asthma pulmonary fibrosis, gastroduodenal ulcers urinary track disorders etc., thus treating will include screening *in vitro* and *in vivo* to determine the effect of the compound on the specific disease. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The

instant claimed invention is unpredictable as discussed below: Many drugs may be potentially useful in the treatment of chronic obstructive pulmonary disease (COPD), but relatively few become available for human use due to lack of safety, lack of efficacy, or both. This is an inherent risk in the drug development process, which coupled with the limited understanding of the molecular pathogenesis of COPD, has produced a trend toward improving existing compounds rather than to develop new compounds. (see abstract *Respiration* 2005;72:105-112).

Thus, in the absence of a showing of correlation between all the conditions associated with the claimed pharmaceutical compound as capable of being treated by compounds of the instant claims, one of ordinary skill in the art is unable to a' prion' predict possible results from the administration of the compounds due to the unpredictability of the role of M3 muscarinic receptor antagonist solely from the structure of the active agent.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation. One of ordinary skill in the art would first need to determine the type of conditions associated with M3 muscarinic acetylcholine receptor antagonist, and then determine which of the thousands of compounds would be suitable for said treatment. Due to the unpredictability in the pharmaceutical art (see reference BMC Pharmacology 2005 5:8), it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

4) Level of predictability in the art.

The art pertaining to the treatment of all types of chronic obstructive lung disease, chronic bronchitis, asthma pulmonary fibrosis, gastroduodenal ulcers urinary track disorders etc. remain highly unpredictable. As disclosed above, there is no absolute predictability even in view of the seemingly high level of skill in the art. Firstly, for a compound or genus to be effective against treatment of chronic obstructive lung disease, chronic bronchitis, asthma pulmonary fibrosis, gastroduodenal ulcers urinary track disorders etc., for example with claimed compound generally unpredictable. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the conditions associated with COPD varies. Accordingly, treatments for preventing with the claimed compound are normally tailored to the particular type of of mediator present, as there is no, and there can be no "magic bullet" against all types of COPD for example.

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is not found in the specification for the treatment of all the diseases listed and claimed in claim 6. However, the gap between the teaching in the specification of *in vitro* activity and *in vivo* is large enough to warrant thorough and compelling *in vivo* data especially in the absence of working examples demonstrating the full scope of all types of disease in claim 6.

6) Existence of working examples.

As discussed above, no working example is found. Applicant's omission of working examples does not enable one of ordinary skill in the art to treat the numerous amounts of diseases encompassed by the instant invention.

7) Breadth of claims.

Claim 1 is extremely broad due to the vast number of possible compound encompassed by the instant invention and the types of disease claimed in claim 6.

8) Level of ordinary skill in the art.

Due to the unpredictability in the pharmaceutical art (see reference BMC Pharmacology 2005 5:8) i.e., having to test every compound, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity. Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of any disease. As a result necessitating one of ordinary skill in the art to perform an exhaustive search to determine which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
4/28/06

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